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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/972,301	11/18/97	COLEMAN	325800-588(P)

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EXAMINER
KEMMERER, E

ART UNIT	PAPER NUMBER
1646	16

DATE MAILED: 01/07/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/972,301

Applicant(s)
Coleman et al.

Examiner
Elizabeth C. Kemmer r

Group Art Unit
1646



☒ Responsive to communication(s) filed on 3 Dec 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 57-61, 71, 74, and 77-89 is/are pending in the applicat

Of the above, claim(s) 79-88 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 57-61, 71, 74, 77, 78, and 89 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims 57-61, 71, 74, and 77-89 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 14

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The request filed on 03 December 1999 (Paper No. 11) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/972,301 is acceptable and a CPA has been established. An action on the CPA follows.

The amendment filed 03 December 1999 (Paper no. 12) has been entered in part. The portion of the amendment requesting that the specification be amended to refer to the present Continued Prosecution Application (CPA) as a continuation of application of Application No. 08/972,301 has not been entered. As set forth in 37 CFR 1.53(d)(7), a request for a CPA is the specific reference required by 35 U.S.C. 120 to every application assigned the application number identified in such request. Thus, there is no need to amend the first sentence of the specification to refer back to the prior application and any such amendment shall be denied entry.

The sequence listing submitted 03 December 1999 has been found to be free of errors and has been entered into the file.

Newly submitted claims 79-88 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the elected invention is directed to polypeptides relating to EMAP III (see Paper No. 3, 14 May 1998 for original restriction requirement; see Paper No. 6, 12 November 1998 for affirmation of the original telephone election). Newly submitted claims 79-88, directed to polynucleotides relating to EMAP III as well as vectors and host cells comprising same, are independent and distinct from the elected polypeptide. The

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polypeptide can be prepared by processes which are materially different from recombinant DNA expression, such as by chemical synthesis, or by isolation and purification from natural sources. Additionally, the polynucleotides can be used other than to make the polypeptide, such in gene therapy or as a probe in nucleic acid hybridization assays. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 79-88 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-56, 62-70, 72, 73, 75 and 76 are canceled. Claims 79-88 are withdrawn from consideration. Claims 57-61, 71, 74, 77, 78 and 89 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The application is now fully in compliance with the sequence rules, 37 CFR 1.821-1.825.

35 U.S.C. § 112, First Paragraph

Claims 57-61, 71, 74 and 89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

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invention. The basis for this rejection is set forth at pp. 3-5 of the previous Office Action (Paper No. 10, 17 June 1999).

Applicant's arguments (pp. 4-6, Paper No. 12, 03 December 1999) have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant argues that the specification need not disclose all the uses of a claimed invention, nor need it disclose matter which was known to persons skilled in the relevant art. Applicant urges that the specification states that EMAP III can be used (1) to regress neoplasia due to its anti-proliferative and anti-angiogenic effects; (2) in a diagnostic assay for detecting altered levels of EMAP III in various tissues; or (3) as an immunogen to produce antibodies. This is not found to be persuasive, because the first use {(1) above} is unsupported by the disclosure. No activity or tissue specific pattern of expression is disclosed for EMAP III which would link it to neoplasia, or would convince the skilled artisan that EMAP III has anti-proliferative or anti-angiogenic activity. In other words, no nexus between neoplasia and EMAP III has been established. As for the second use {(2) above}, since no tissue specific pattern of expression has been disclosed for EMAP III, and no tissues showing altered EMAP III expression for any reason have been disclosed, the skilled artisan would have to resort to trial and error to identify particular tissues at particular developmental stages or in a particular disease state which show altered EMAP III expression. Such trial and error experimentation, in the absence of any guidance by the specification, is considered undue. Regarding the third use {(3) above}, since the skilled artisan would not know how to use EMAP III, it follows that the skilled artisan would not know how to use an EMAP III antibody. For example, no tissues

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specific pattern of expression has been established, thus, the antibody cannot be used to identify different tissues.

Applicant also argues that no experimentation is required to enable the skilled artisan to use the claimed invention in a manner similar to EMAP II, such as to activate endothelial cells and mononuclear cells to potentiate their participation in procoagulant reactions through induction of tissue factor, or to promote migration of monocytes and polymorphonuclear leukocytes, both of which are known in the art. This is not found to be persuasive, because the structural similarity between EMAP II and EMAP III cannot lead the skilled artisan to infer a functional similarity in the absence of supporting evidence. As stated in the previous Office Action, the relevant literature reports examples of closely related polypeptides belonging to a polypeptide family wherein individual members have distinct, and sometimes even opposite, activities. For example, Tischer et al. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences between PDGF and VEGF are also seen *in vivo*, wherein endothelial-pericyte associations in the eye are disrupted by intraocular administration of PDGF but accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598; see Abstract and pp. 1594-1596). In the transforming growth factor (TGF) family, Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF- β family of proteins, has the ability to

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induce metanephrogenesis, whereas closely related TGF- β family members BMP-2 and TGF- β 1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). See also Massague, who reviews other members of the TGF- β family (1987, Cell 49:437-8, esp. p. 438, column 1, second full paragraph to the end). Similarly, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone 14:717-720; see p. 717, second paragraph of Introduction). Finally, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48).

Therefore, due to the large quantity of experimentation necessary to determine an activity or property of EMAP III such that it can be determined how to use EMAP III, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the state of the prior art establishing that biological activity cannot be predicted based on structural similarity, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claim 89 is rejected under 35 U.S.C. 102(b) as being anticipated by Creative Biomolecules, Inc. (WO 92/15323; hereinafter referred to as "Creative"). Creative teaches mature forms (part (e) of claim 89) of secreted proteins as well as full length (part (f) of claim 89) secreted proteins (osteogenic proteins; see p. 11 and Table II). Any of these meet the limitations of a "variant" of SEQ ID NO: 2 as recited in part (g) of claim 89, since no structural or functional limitations are set forth in part (g) of claim 89.

Conclusion

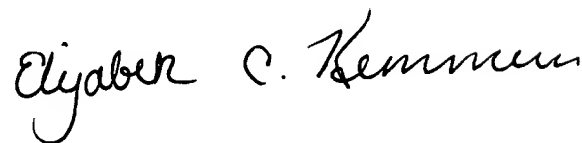
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D., whose telephone number is (703) 308-2673. The examiner can normally be reached on Mondays through Thursdays from 6:30 a.m. to 4:00 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



**ELIZABETH KEMMERER
PRIMARY EXAMINER**

ECK
January 6, 2000